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09/576,715	05/23/2000	Kazuhisa Hatakeyama	2000 0644A	3112

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EXAMINER
FORMAN, BETTY J

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/576,715	Applicant(s) HATAKEYAMA, KAZUHISA	
	Examiner BJ Forman	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 7 January 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/576,715 is acceptable and a CPA has been established. An action on the CPA follows.

2. This action is in response to papers filed 30 November 2001 in Paper No. 13 in which claims 1 and 10-13 were amended and claim 9 was canceled. All of the amendments have been thoroughly reviewed and entered. The previous rejections of Claims 1-12 in the Office Action of Paper No. 11 dated 6 August 2001 are withdrawn in view of the amendments. The previous rejection of Claim 13 is maintained. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Currently claims 1-8 and 10-13 are under prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-8 and 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-8 and 10-12 are indefinite in Claim 1 because the claims are drawn to methods of gene analysis but the method does not recite analytical steps. Therefore, it is

unclear what gene analysis is being claimed. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested that Claim 1 be amended to recite positive and active steps of gene analysis e.g. detecting deleted regions (page 18, lines 25-26) detecting the presence or absence of a mutation (page 19, lines 15-17) mapping gene location (page 19, lines 24-25) detecting mismatch and complete match (page 25, lines 7-21).

b. Claims 10-12 are each indefinite for the recitation "the intensity of a hybridization signal obtained form the hybridization" because "intensity" and "hybridization signal" both lack antecedent basis in Claim 1. It is suggested that the claims be amended to provide proper antecedent basis e.g. in Claim 1, line 14, following fluorescent substance" insert "thereby producing a hybridization signal having a hybridization signal intensity".

c. Claims 10-12 are each indefinite for the recitation "each hybridization signal being represented by the presence of said fluorescent substance" because "represented by" is a non-specific relational phrase and therefore the relationship between the "hybridization signal" and the "fluorescent substance" is undefined. It is suggested that the claims be amended to define the relationship e.g. replace "being represented by" with "identifies".

d. Claim 11 is indefinite for the recitation "detecting the polymorphism" because "polymorphism" lacks proper antecedent basis in Claim 1. It is suggested that Claim 11 be amended to provide proper antecedent basis e.g. replace "the" with "a".

e. Claims 11 and 12 are each indefinite for the recitation "wherein the detection of the hybridization is performed by using a plurality of probe nucleic acids" because it is unclear whether the "plurality of probe nucleic acids" are used in addition to the probe nucleic acids in the first "providing" step of Claim 1 or are used only during the detection step of Claim 1. The

recitation is further indefinite because it is unclear how the plurality of probes are used. It is suggested that Claims 11 and 12 be amended to clarify e.g. replace "wherein the detection of the hybridization is performed by using" with "further comprising".

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Weininger et al. (U.S. Patent No. 5,871,902, issued 16 February 1999).

Regarding Claim 1, Weininger et al. disclose a method of gene analysis by detecting hybridization between a probe nucleic acid (PNA) and a sample nucleic acid (TNA) comprising a target sequence (TBR) complementary to that of the probe nucleic acid comprising: immobilizing either the probe nucleic acid or the sample nucleic acid; adding the other probe or sample nucleic acid to the immobilized nucleic acid wherein either the probe or sample nucleic acid is labeled; performing hybridization in the presence of a double-stranded DNA-binding protein having the function to stabilize a complementary double-stranded DNA; and detecting the label to thereby detect hybridization of the probe and sample nucleic acid (Claim 2) wherein the label is fluorescent substance (Column 1, lines 26-33) and wherein gene analysis is performed via the method i.e. the TNA comprise foreign genes, defective genes (Column 17, lines 45-54).

Regarding Claim 2, Weininger et al. disclose the method wherein the sample nucleic acid is DNA (Column 9, lines 43-44).

Regarding Claim 13, Weininger et al. disclose a kit for detecting hybridization between a probe and sample nucleic acid comprising a double-stranded DNA-binding protein (Claim 32). The claim is drawn to a kit comprising a double-stranded DNA-binding protein having the function to stabilize a complementary double-stranded DNA. The intended use of the kit i.e. "for detecting hybridization ... according to the method of Claim 1" is not given any patentable weight. The courts have stated that a preamble is generally not accorded any patentable weight where it merely recites the intended use, and where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone (see *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d at 152, 88 USPQ at 481). In the instant case, the preamble is not accorded any patentable weight because it merely recites the intended use for the kit and because the components of the kit i.e. a double-stranded DNA-binding protein having the function to stabilize a complementary double-stranded DNA, is able to stand alone and is capable of performing the intended use. Weininger et al. disclose the kit as claimed.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 3-8 and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Weininger et al. (U.S. Patent No. 5,871,902, issued 16 February 1999) in view of Guagliardi et al. (Journal of Molecular Biology, 1997, 267: 841-848) and SwissProt (Accession No. 059631, 15 December 1998 and Accession No. P39476; P81550, 1 February 1995).

Regarding Claim 3, Weininger et al. teach a method of gene analysis by detecting hybridization between a probe nucleic acid (i.e. PNA) and a sample nucleic acid (i.e. TNA) comprising a target sequence (i.e. TBR) complementary to that of the probe nucleic acid comprising: immobilizing either the probe nucleic acid or the sample nucleic acid; adding the other probe or sample nucleic acid to the immobilized nucleic acid wherein either the probe or sample nucleic acid is labeled; performing hybridization in the presence of a double-stranded DNA-binding protein (i.e. TBA) having the function to stabilize a complementary double-stranded DNA; and detecting the label to thereby detect hybridization of the probe and sample nucleic acid (Claim 2) wherein the label is fluorescent substance (Column 1, lines 26-33) and wherein gene analysis is performed via the method i.e. the TNA comprise foreign genes, defective genes (Column 17, lines 45-54) and wherein the double-stranded DNA-binding protein (i.e. TBA) is selected for optimization of stability (Column 9, lines 47-63) but the do not teach the DNA-binding protein is derived from a hyperthermophilic bacterium. However, hyperthermophilic bacteria were known in the art at the time the claimed invention was made a taught by Guagliardi et al. who teach a similar method of gene analysis comprising: hybridizing a probe nucleic acid and sample nucleic acid in the presence of a double-stranded DNA binding protein derived from a hyperthermophilic bacterium and detecting the hybridization (page 842, Fig. 1) wherein said protein stabilizes complementary double-stranded DNA and promotes hybridization (Abstract) and wherein the promotion of hybridization is "strictly homology dependent" whereby a single mismatch "severely reduces hybridization efficiency" (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to DNA-binding protein of Weininger et al. with the DNA-

binding protein derived from a hyperthermophilic bacterium of Guagliardi et al. to thereby differentiate between perfect-match and single mismatch hybridizations as taught by Guagliardi et al. for the obvious benefit of differentiating and detecting single-base mismatches known to be associated with clinically important diseases e.g. sickle cell anemia.

Regarding Claim 4, Guagliardi et al. teach the method wherein the double-stranded DNA-binding protein is derived from an archaebacterium (page 841, right column, first full paragraph).

Regarding Claim 5, Guagliardi et al. teach the method wherein the double-stranded DNA-binding protein is derived from a bacterium belonging to the genus *Sulfolubus* (page 841, right column, first full paragraph).

Regarding Claim 6, Guagliardi et al. teach the method wherein the double-stranded DNA-binding protein is derived from *Sulfolubus solfataricus* (page 841, right column, first full paragraph).

Regarding Claim 7, Guagliardi et al. teach the method wherein the double-stranded DNA-binding protein is the Sso7d protein derived from *Sulfolubus solfataricus* (page 841, right column, first full paragraph).

Regarding Claim 8, Guagliardi et al. teach the sequence of the Sso7d is known (page 841, right column, lines 9-18) and SwissProt specifically teaches the sequence accession No. 059631; P39476; and P81550).

Regarding Claim 10, Weininger et al. teach the method wherein the target nucleic acid is detected with accuracy even in the presence of closely related but different sequences (Column 1, lines 9-13) but they do not specifically teach the amount of the sample is analyzed based on the intensity of a hybridization signal. However, Guagliardi et al. teach the similar method wherein the amount of target sequence is analyzed i.e. the intensity of the labeled nucleic acids bound and unbound to the DNA-binding proteins is analyzed to determine the amount of nucleic acids bound (% annealed product) (page 844, Fig. 2b and page 845, Fig. 3a

and Fig. 4a). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the detection of Weininger et al. and to analyze the amount target based on the intensity of signal produced as taught by Guagliardi et al. to thereby identify samples having the highest homology to a probe having a disease-specific sequence for the expected benefit of accurately identifying and diagnosing the disease as taught by Guagliardi et al. (page 847, right column, lines 6-14).

Regarding Claim 11, Weininger et al. teach the method comprising a plurality of probe nucleic acids (Column 12, lines 1-6) wherein the target nucleic acid is detected with accuracy even in the presence of closely related but different sequences (Column 1, lines 9-13) and they teach defective genes are detected (Column 17, lines 45-50) but they do not specifically teach a polymorphism is detected based on the hybridization signal. However, Guagliardi et al. teach the similar method wherein the detection of hybridization is performed by using a plurality of probe nucleic acids and detecting the polymorphism in the target sequence by comparing the hybridization signal obtained from the hybridization (page 844, right column, first paragraph and page 845, Fig. 4) and wherein the intensity of each hybridization signal is obtained and compared (page 845, Fig. 4, and page 842, Fig. 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the defective gene detection in the method of Weininger et al. by detecting a polymorphism which is defective gene and to thereby detect clinically important disease resulting from polymorphism e.g. sickle cell anemia for the expected benefit quickly and accurately diagnosing clinically important diseases as suggested by Guagliardi et al. (page 847, right column, lines 6-14).

Regarding Claim 12, Weininger et al. teach the method comprising a plurality of probe nucleic acids (Column 12, lines 1-6) wherein the target nucleic acid is detected with accuracy even in the presence of closely related but different sequences (Column 1, lines 9-13) but they do not specifically teach detecting nucleic acid sequence based on the hybridization signal. Guagliardi et al. teach the method wherein the detection of hybridization is performed using a

plurality of probes and detecting nucleotide sequence by comparing the hybridization signal (page 844, right column, first paragraph and page 845, Fig. 4) and wherein the intensity of each hybridization signal is obtained and compared (page 845, Fig. 4, and page 842, Fig. 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the defective gene detection in the method of Weininger et al. by detecting the nucleic acid sequence as taught by Guagliardi et al. to thereby identify samples the highest homology to a probe having a disease-specific sequence for the expected benefit of accurately identifying and diagnosing the disease as taught by Guagliardi et al. (page 847, right column, lines 6-14).

9. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guagliardi et al. (M. Mol. Bio. 1997, 267: 841-848) in view of Stratagene (catalog, 1988, page 39). The claim is drawn to a kit comprising a double-stranded DNA-binding protein having the function to stabilize a complementary double-stranded DNA. The intended use of the kit i.e. "for detecting hybridization ... according to the method of Claim 1" is not given any patentable weight. The courts have stated that a preamble is generally not accorded any patentable weight where it merely recites the intended use, and where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone (see *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d at 152, 88 USPQ at 481). In the instant case, the preamble is not accorded any patentable weight because it merely recites the intended use for the kit and because the components of the kit i.e. a double-stranded DNA-binding protein having the function to stabilize a complementary double-stranded DNA, is able to stand alone and is capable of performing the intended use.

Regarding Claim 13, Guagliardi et al. teach the claimed reagents for detecting hybridization between a probe nucleic acid and a sample nucleic acid comprising: a target sequence complementary to the probe nucleic acid and a double-stranded DNA-binding protein which functions to stabilize complementary double-stranded DNA (page 482, Fig. 1) but they do not teach the reagents combined into a kit. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Guagliardi et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Response to Arguments

10. Applicant argues that instant Claim 13 is not obvious in view of Guagliardi et al. and Stratagene because the claim has been amended to depend from Claim 1 and because Guagliardi et al. do not teach all the limitations recited in Claim 1. The argument has been considered but is not found persuasive for the reason stated above i.e. the intended use of the kit i.e. "for detecting hybridization ... according to the method of Claim 1" is not given any patentable weight. The courts have stated that a preamble is generally not accorded any patentable weight where it merely recites the intended use, and where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone (see *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d at 152, 88 USPQ at 481). In the instant case, the preamble is not accorded any patentable weight because it merely recites the intended use for the kit and because the components of the kit i.e. a double-stranded DNA-binding protein having the function to stabilize a complementary double-stranded DNA, is able to stand alone and is capable of performing the intended use.

Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Linn et al. (U.S. Patent No. 5,641,633, issued 24 June 1997) teach a method of gene analysis by detecting hybridization between a probe nucleic acid and a sample nucleic acid comprising a target sequence complementary to that of the probe nucleic acid comprising: adding the probe nucleic acid to the sample nucleic acid; performing hybridization in the presence of a double-stranded DNA-binding protein having the function to stabilize a complementary double-stranded DNA; and detecting the hybridization of the probe and sample nucleic acid (Column 4, lines 19-41 and Claim 1) wherein the probe nucleic acid is labeled with a fluorescent substance (Column 5, lines 3-11) wherein detecting hybridization comprises detecting the presence of the labeled substance (i.e. change in fluorescence, Column 6, lines 4-21) and wherein the probe or sample nucleic acid is DNA (Example 1, Column 10, line 17-Column 11, line 27)

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1655
January 24, 2002